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CARCINOMA IN EARLY LIFE.*

WITH SPECIAL REFERENCE TO EARLIER METHODS IN
INTRA-VITAM DIAGNOSIS.

BY WALTER L. BIERRING, M.D.

Professor of Pathology and Bacteriology, State University of Iowa;
Pathologist to the University Hospital.

IOWA CITY, IOWA.

Carcinoma is usually regarded as the malignant tumor of later life, having its legitimate age limit at 35, though it is most frequently met with after 40 years of age.

With increasing study of the malignant neoplasms, age is gradually losing its hold as a criterion of difference between sarcoma and carcinoma, the former being found at almost any age, while carcinoma is beginning to be noticed more frequently during the earlier decades of life.

Having had the opportunity of examining the material from nine cases of carcinoma between the ages of 23 and 35 years, I have incorporated the same in the subject of my paper, and drawn from them such points as were of pathologic interest.

CASE 1.—MRS. A. F. R., presented herself in the private practice of Dr. L. W. Littig, who has kindly furnished the clinical data. She was admitted to University Hospital, Dec. 6, 1898, and was 23 years old, married, and had one child 3 years old. The family history as regards tuberculosis and neoplasms was negative. Her health was good to within six months of admission, after which time she had pain in the pelvic region and offensive discharge from the vagina.

Physical examination of the thoracic and abdominal organs, with the exception of the uterus gave negative results; vaginal examination revealed an indurated, warty, slightly ulcerating growth involving the cervix uteri, extending a short distance on to the anterior and posterior vaginal walls; displacement of the uterus did not exist.

A clinical diagnosis of epithelioma of the cervix uteri was proposed and operative removal advised. Following operation, Dec. 8, 1898, of abdominal hysterectomy, unfavorable post-operative symptoms appeared, except a rather unusual interference in the complete healing of the abdominal incision, by the appearance, a short time after the operation, at the site of suture wound, of a papillomatous, granuloma-like growth which gradually increased in size and within five months presented a warty ulcerating growth the size of a lemon, which had all the macroscopic characteristics of a surface carcinoma or epithelioma. This growth was removed by a second operation on May 11, 1899.

The examination of the uterine growth revealed a complete involvement of the cervix uteri by the tumor

mass, which presented a histology of delicate fibrous stroma separating irregular, narrow bands or rows of pavement epithelial cells, the latter showing numerous karyokinetic figures, and at the edges of the tumor area, indications of extensive infiltration into the muscular structure of the corpus uteri. The diagnosis was carcinoma.

The microscopy of the secondary growth removed from the site of abdominal incision presented a similar arrangement of large, irregular alveoli of pavement epithelial cells, enclosed by a delicate fibrous connective tissue stroma like that in the primary growth.

CASE 2.—This case was in the service of Dr. J. C. Shrader, at Mercy Hospital, in Mrs. M. G., aged 26 years, married, with no children. Her family history as regards cancer was negative. Her general health was good, but during the past five years she had been annoyed by pruritus of the external genitals, accompanied by the slow development of a warty, ulcerating growth at the point of irritation.

Physical examination revealed an ulcerated, painful area on the left labium majus, with papillomatous, indurated edges, being $1\frac{1}{2}$ inches long by $\frac{3}{4}$ inch in width; two enlarged lymph nodes were noted in the left inguinal region.

Operation for removal of primary growth and involved lymph nodes was performed Nov. 15, 1897, and there has been no recurrence to date.

The microscopic examination revealed the typical picture of epithelial proliferation from the surface, and formation of distinct nests or pearls of pavement epithelial cells in the deeper tissues as common to, and indicative of, squamous-cell epithelioma.

CASE 3.—This case occurred in the service of Dr. J. W. Dalbey, in the University Hospital, in O. E. C., a male laborer, aged 28 years, and single. His family history as regards cancer was negative. The right lower eyelid presented an ulcerated area three-quarters by one-half inch, with proliferated edges, which, according to the patient, had been gradually developing during the past five years. This was removed by operation on July 6, 1899, primary union following and no recurrence.

Microscopy revealed irregular columns of pavement epithelial cells extending down from the surface, with well-marked epithelial nests, beneath the surface, giving the characteristic histologic picture of pavement-celled epithelioma.

CASE 4.—The patient was seen in the medical service of Dr. L. W. Littig, in the University Hospital, viz.: R. R. T., aged 30 years, a farmer and single. When presented, Nov. 9, 1897, he gave a history of indefinite symptoms with reference to disturbances in digestion, and distress in the epigastric region; during the two months previous to entrance he had noticed a tumor-like enlargement below the left rib-border. There was no marked localized pain.

Physical examination of the thoracic organs was neg-

*Read before the Des Moines Pathological Society, Nov. 14, 1899.

ative; in the epigastric and left hypochondriac regions a defined area of dulness was noticeable, having a transverse diameter of $3\frac{1}{2}$ inches, palpation revealing a movable, circumscribed growth not influenced by respiratory movement, and separable from the hepatic and splenic areas of dulness.

A diagnosis of tumor abdominalis was proposed, the nature of this by reason of the age of the patient, being left indefinite, and exploratory operation advised. The latter was not granted and the patient passed from observation until death occurred, Feb. 8, 1898.

The post-mortem examination, by request of the relatives, was confined to the abdominal cavity. General emaciation was very marked; panniculus adiposus was greatly diminished. On opening the abdomen a large mass the size of a child's head was found involving the greater curvature of the stomach and the transverse colon; the mass, with adherent organs, was removed; the liver presented a high grade of fatty infiltration but no evidence of metastatic involvement; the spleen was not enlarged, and the kidneys were negative.

Closer examination of the tumor mass showed such an intimate connection with both the large intestine and the stomach as to render it difficult to distinguish from which organ it had its origin. The mucous surface of the stomach was smooth, the wall presenting a diffuse thickening which gradually merged into the tumor mass. In the lumen of the transverse colon extensive ulceration was noted corresponding to the tumor area.

In the microscopic section, representing a section through the mucous membrane of the stomach and into the substance of the tumor mass, the mucous membrane appears atrophic, and the tubular glandular structure is almost obliterated; in the submucosa, irregular tubules are seen, filled with cubical epithelial cells; deeper, elliptical and oval alveoli are noticeable, filled with cells, while narrow columns of cells—sometimes composed of single rows of cells—are seen radiating and infiltrating the fibrous stroma in all directions. Fatty degeneration in the larger cell collections is noted, and numerous karyokinetic figures are seen. The diagnosis was adenocarcinoma, most probably of stomach origin.

CASE 5.—This occurred in a patient of Dr. W. D. Middleton, at the University Hospital, viz.: W. R., aged 32 years, also a farmer and single. When admitted, he presented a large, ulcerating growth of the right side of the face, extending down on to the side of the neck for a distance of two inches, exposing the inferior maxillary bone in several places; the growth was of two years' standing. Microscopic section of particles removed from different portions of the growth gave a typical picture of epithelioma.

Coley's mixture of erysipelas and prodigious toxins was used in the therapy without appreciable benefit and the patient died in the hospital, two months after entrance. An autopsy was not granted.

CASE 6.—This case occurred in the practice of Dr. R. W. Hill, Davenport, Iowa, to whom I am indebted for the following: Mrs. N., aged 34 years, gave a history of several years of constipation, leading to almost complete obstruction when first observed by the attending physician. There was no emaciation, no localized pain, no distinct tumor, but a stenosis due to neoplasm was diagnosed and operation advised.

Laparotomy revealed an obstruction of the descending colon just above the junction with the sigmoid flexure, due to a neoplastic growth encircling the intestine. Resection was performed, removing about five inches of the colon and sigmoid flexure, the end of the descending

colon being fastened to the abdominal wall, to form an artificial anus, while the resected end of the rectum was inverted upon itself. Death occurred five days after operation, from peritonitis.

The gross pathologic appearance of the resected portion of intestine reveals a dense tumor mass enveloping the lumen of the intestine to the extent of two inches, constricting the same so that it admits but the passing of a finger; the entire growth being about the size of a lemon. No ulceration of the mucous surface is present; the cut surface of the tumor presents a dense structure in which numerous areas of mucilaginous softening are noticeable.

Microscopic examination of a section including mucous membrane and a large extent of the growth proper, shows no change in the mucosa, but in the submucous area are noted numerous oval-shaped alveoli more or less completely filled with short columns or cubical epithelial cells. Aside from the alveoli, areas are noted which are quite devoid of cells, and are filled instead with a delicate fibrous material giving the reaction of mucin. The stroma of fibrous connective tissue shows but slight retrograde change. A diagnosis of acinous carcinoma undergoing extensive myxomatous degeneration, was made.

CASE 7.—Miss G. W., aged 34 years, a dressmaker, was admitted Jan. 4, 1899, to the surgical service of Dr. W. D. Middleton, at the University Hospital. Her family history with reference to cancer was negative, and her health good until one year ago, when a small lump was noticed in the right breast, which rapidly enlarged and has been accompanied by sharp lancinating pains.

Physical examination revealed a large, rather circumscribed, slightly movable tumor mass involving the entire area of the right mamma; the surface about the nipple was retracted and over the gland proper, broken by numerous sinuous openings from which milky purulent-like discharge was escaping.

Operation was performed Jan. 5, 1899, comprising extirpation of the tumor and the gland, with three enlarged axillary lymph-nodes.

The cut surface of the tumor presents a growth of semisolid consistency, extending in various directions from the nipple into the substance of the gland, the size of the tumor being about that of a small coconut.

Microscopic sections stained in hematoxylin and eosin method, and by Van Gieson's method, reveal elliptical, oval, and irregular alveoli filled with cubical epithelial cells, surrounded by bands of dense fibrous tissue, the fibrous stroma and cell collections being about evenly distributed. The stroma presents occasional small areas of mucoïd degeneration. Central areas of cells in the larger alveoli show marked granular and fatty changes. Numerous karyokinetic figures are seen throughout the cell areas. A diagnosis of acinous carcinoma was made.

On March 8, 1899, a secondary recurrent nodule of chestnut size, was removed from the site of the scar of the first operation, and possessed the same structural characters as the primary growth.

CASE 8.—This case occurred in the surgical service of Dr. W. D. Middleton; admitted Feb. 1, 1899. Mr. J. A. G., aged 35 years, married, jeweler, gave no family history of carcinoma, but a history of an attack of acute articular rheumatism of six months' duration, two years preceding admission; during this severe abdominal pain was a prominent symptom. Eight weeks previous to admission he noticed a palpable swelling just below the rib-border in the right mammary line. When first noticed it was of the size of a hen's egg, but gradually enlarged

and was the site of considerable pain which radiated out into the abdomen. Emaciation and anemia were marked.

Physical examination of the thoracic organs gave a negative result. In the right hypochondriac region a palpable, movable tumor, orange-size, was felt. Percussion showed it as not separable from the liver area of dulness, and influenced by respiratory movements. There was no icterus, constipation, nor ascites. Exploratory operation was performed Feb. 21, 1899, by Dr. Middleton, and revealed, on exposure of the abdominal structures, a large tumor mass the size of a child's head, in the region of, and apparently originating in, the hepatic flexure of the colon, and adherent to the under surface of the liver and pyloric extremity of the stomach. The extensive adhesions precluded any possibility of removal, and the abdominal wound was closed after removing from the most prominent and accessible portion of the tumor two small pieces for microscopic examination. A histologic section revealed the picture of adenocarcinoma.

The patient, shortly after operation, returned to his home in northern Iowa, where death occurred within three months. An autopsy was not obtained.

I wish to add to the foregoing an interesting instance of early carcinoma which recently came to my notice in the practice of Dr. G. L. Day, Lone Tree, Iowa. Mrs. W., aged 27, married. Soon after the birth of her child two years ago, a nodular ulcerating growth was noted by the attending physician in the upper part of the rectum. During the last year hemorrhagic ascites prevailed, and in three different tappings sixteen liters of fluid were removed. Death occurred Nov. 21, 1899. Autopsy revealed a most extensive carcinomatosis of the peritoneal cavity, to which the metastasis was confined; the abdominal structures were all adhered and matted together into one dense mass, the infiltrated omentum having a thickness of two inches. The primary growth in the rectal wall and metastatic manifestations presented the typical macroscopic and microscopic appearance of adenocarcinoma with accompanying myxomatous degeneration.

In the list of examples of early carcinoma noted, the ages 23, 26, 27, 28, 30, 32, 34 and 35 years are represented. Four of the growths had their origin from surface epithelioma and five from glandular epithelial cells.

Of the cases recorded in literature, intestinal carcinomata have been most frequently observed, but involvement of other tissues common to cancer has been reported by trustworthy observers. Since the publication of Mathieu's classic article, in 1884, it has been more generally admitted than before that cancer of the stomach can occur before the age of 35, once regarded as the earliest possible period. Mathieu² himself reported, in 1895, a case of cancer of the stomach in a man 25 years of age. Dock³ has reported two cases of the same affection occurring at 20 and 24 years of age. In a review of carcinoma developing from dermoid cysts of the ovarian region, J. G. Clark⁴ cites three cases at 21, 26 and 29 years respectively. A most remarkable series of precocious cancer is reported by de la Camp,⁵ including 4 cases of a carcinoma ovarii in a girl of 19 years, carcinoma ventriculi in a boy of 14, and 1 of 16 years of age, also a case of carcinoma of the colon in a boy of 16. This author at the same time made a careful search of the literature on the subject, collecting 9963 cases, and of these 19 occurred before 20 years of age. W. Roger Williams¹⁵ collected the record of 11,934 cases,

and found 0.99 per cent occurring before 30 years, and 2.36 per cent. before 35 years of age. Cumston⁶ recently reported 3 cases at 19, 24 and 28 years, occurring in the liver, uterus and ascending colon. A Trayer (*Correspondenz Blatt für Schweizer Aerzte*, Oct. 15, 1899) reported the rare occurrence of carcinoma of the kidney in a man 20 years of age. Many cases are published in so casual a way that enumeration and analysis are out of the question.

Carcinoma in early life often has a slow course, and like that of later years may be latent for a considerable length of time. That cancer in early life is becoming more frequent is very evident; whether it keeps pace with the general increase in carcinoma will be difficult to determine. Certainly a collective study of the statistics reveals the unfortunate fact that the mortality rate of carcinoma is on the increase. Roswell Park⁷ calls attention to the statistics of New York State, showing 2363 deaths in 1887 against 4456 in 1898. In England and Wales, where careful records are kept, the rate of occurrence of cancer has increased from 1 in 5646 population in 1840 to 1 in 1306 in the year 1896, an increase of five times in fifty years. This increase can hardly be ascribed as due to improvements in methods of diagnosis, for rather the reverse is the case, since many cases which were formerly diagnosed as cancer are now properly classified where they belong in other lists.

While the etiology of cancer remains obscure, there is but little hope that the future will offer any abatement in this progressive increase. As careful observation continues to note the occurrence of carcinoma in the earlier decades of life, there is removed from the list of predisposing causes, the influence of age.

It has been an attractive explanation to attribute to the lessened physiologic resistance in connective tissue the rôle of permitting atypical proliferation of epithelium beyond its normal limits. With advancing age the submucous, subcutaneous and interstitial connective tissues undergo atrophic changes, while the covering or lining epithelial elements seem to retain their usual vitality. When glands reach the limit of their functional rôle in the organism, the danger from carcinoma is most marked, while it diminishes again when complete atrophy has taken place. When cancer occurs thus in the developing decades of life, the above influences can hardly be considered.

Bearing on the subject of etiology I must refer again to the peculiar secondary, recurrent growth, noted in Case 1. The removal of the primary growth, with uterus and appendages, was technically as perfect as it could possibly be in any case. There was not the slightest involvement of the peritoneal cavity, and yet, shortly after the operation, there appeared in the abdominal suture wound a secondary tumor, identical in structure with the primary one. The nature of the constituent elements left no doubt as to its metastatic nature, yet if a similar instance were to occur in connection with any of the infections how readily it would be explained. While I do not pretend to advance this as any direct evidence of a parasitic cause or spread of living virus, it does seem to me to mean more than the simple transmission of active epithelial cells from primary to secondary site.

In the entire field of pathology, no subject has proven more alluring to physician and investigator than the etiology of carcinoma. It was no wonder that the development of bacteriologic methods gave a mighty impetus to the search for an etiologic agent, the result of which is well known. Numerous forms of cell inclusions—cancer bodies—have been observed and variously

interpreted. Renewed and repeated attempts have been made to find the curative agent among the protozoa which are to enter the cells and render the same infective. Such workers as Hansemann, Rippert and Schwarz have continued to oppose any such adoption, and it would seem as if that most careful and critical work of Pianese⁸ has about taken the bottom out of the theory. By the use of unique staining methods and very careful technique this painstaking Italian has demonstrated, in proliferating cells, both inflammatory and neoplastic, changes and bodies which appear identical with the various forms of cell-inclusions of other observers, but which are demonstrated to be naught but evidences of different forms of cell degeneration.

An interesting contribution is that of Leyden and Schandinn,⁹ who have found in the ascitic fluid of malignant neoplasms—carcinoma—a new ameba-like body of the family of rhizopoda, which appear as round bodies in the fluid, having clear and yellow granules, with ameboid movement, and pseudopods of unusual length, life and mobility being retained four to five hours after removal on to the slide. The authors do not advance any definite etiologic connection with carcinoma, yet regard their appearance as quite significant.

Italian pathologists, led by Sanfelice¹⁰ and Roncali,¹¹ are still champions of the infectious theory, and their recent publications deal exclusively with certain organisms which they place among the blastomycetes, a familiar example of which is the ordinary yeast plant. They regard the organism which they have isolated from tumors in man, and successfully inoculated into animals, as largely identical with the various bodies long observed and variously interpreted as protozoa, cell inclusions, and later as cell degeneration products. Roswell Park finds the work of the Italian pathologists creditable and convincing, and it is to be expected that the New York State Laboratory, in Buffalo, whose special mission is the investigation of tumors, will soon issue some exhaustive work on the subject. If blastomycetes occur in cancers in Italy, they can probably also be demonstrated elsewhere.

As yet it is evident that the real cause of carcinoma has not been demonstrated. Perhaps it will be necessary to completely modify our culture methods. Perhaps our optical aids are inadequate in magnifying power, but unless the light comes soon, the nineteenth century will close with the genesis of cancer as much a mystery as when the century began.

Carcinoma continues to be a strictly surgical disease, and in this light I have thought it in place to refer to some of the earlier methods applicable in intra-vitam diagnosis, with special reference to the following: 1, characters of cancerous effusions in serous cavities; 2, necessity of an early microscopic examination of tumor particles, and 3, the proper interpretation of the histologic picture.

The early appearance of ascites and effusions in serous cavities involved by carcinoma, renders the fluid a good object for examination. The first scientific contribution on the subject was offered by Rieder,¹² who called especial attention to the cells found in effusions, to which subject Dock¹³ has also added a most interesting article. I have endeavored to carefully examine all effusions from carcinoma cases it has been my privilege to see, and while my material has been somewhat limited, I have noted the various cell forms described by former observers, and have drawn from these studies the following points:

The specific gravity of cancerous effusions is rarely

above 1015, and in that way is distinguishable from tuberculous exudates in which the specific gravity is usually higher, ranging from 1022 to 1025. Since exceptional instances of a lower specific gravity in tubercular pleurisy have been reported, this differential test must be used with a certain caution in diagnosis. The cells are by far the most characteristic feature about the effusion, the most perfect description of these having been furnished by Rieder. Cells having the appearance of lymphocytes are rare; multinuclear leucocytes are uncommon. Cells containing numerous fatty granules are frequent, the accumulation of granular material being confined principally to certain areas in the cells. Giant cells or aggregations of cells are a special feature, some of the former containing twenty to twenty-four nuclei. The most remarkable feature of the sediment is presented by the great number of karyokinetic figures, which are very numerous, presenting as common forms the equatorial plate and anaphase stages; another very characteristic point noted is the presence of atypical mitosis in the larger cells.

Atypical mitosis is an interesting study and has been demonstrated in all active proliferating pathologic processes, but with especial import in carcinoma.

In ordinary serous effusions, as in serous pleurisy and tubercular peritonitis, the large majority of cells are multinuclear leucocytes; furthermore, there are noted numerous small cells having the characters of lymphocytes, a few large mononuclear cells and some fibroblasts. The large cells with mitosis and atypical mitosis seen in cancerous effusions do not, as a rule, have their counterpart in ordinary exudates, which statement bears a slight modification, owing to the reported finding by Dock,¹³ in the exudate of pleurisy, of large cells showing karyokinesis.

As a diagnostic guide, it is necessary to state that the number of cells showing mitosis and asymmetric mitosis in cancerous effusions is much greater than in those of simple or tuberculous inflammation, and by this quantitative distinction, it would be possible to make a differential diagnosis.

The large cells that have been referred to are principally of the type of endothelial ones, resembling cells seen in scrapings from serous surfaces, with the exception that the latter do not show cell-division-figures.

One can hardly hope to determine the exact histologic character of a growth occurring on a membrane, from isolated cells found in the serous effusions. If it were possible to demonstrate the *Leydenia gemmipara*, described by Leyden and Schandinn in cancerous ascitic fluids, an additional aid in diagnosis would be furnished.

MICROSCOPIC EXAMINATION OF TUMOR ELEMENTS.

The value and import of a knowledge of the nature of a growth, previous to surgical interference, must be apparent to every one, especially since it is becoming manifest that carcinoma may occur at almost any age. Portions of tumors can usually be obtained in a large number of cases. Surface carcinomata, both cutaneous and mucous, are accessible. Uterine scrapings are a great aid. Particles may be observed in stomach washings and in the stools and urine.

While the clinical signs in many instances may be very plain, a microscopic corroboration is always desirable. Frequently the specimens examined in this work represent superficial sections, so that certain caution is necessary in correctly interpreting the histologic picture.

Herzog¹⁴ has called attention to a case in which three pieces were removed from a tumor of the larynx, all of which were called fibroma, while the extirpation of half

the larynx revealed the typical picture of carcinoma. The uneven white elevation seen in the larynx in carcinoma may be merely a deposit and infiltration of fibrin.

In examining uterine scrapings I have noted that while a superficial piece might reveal simply a sort of adenomatous hyperplasia, a deeper section furnished the diagnosis of carcinoma. This would apply whenever adenocarcinoma would be likely to develop, and for the differentiation, histologically, of simple adenoma and adenocarcinoma, I would suggest that the following points be noted: 1, presence of atypical adenomatous glands; 2, absorption of stroma and agglutination of the glands in loops of the same gland; 3, the proliferation of the lining epithelium of glands; 4, filling of gland spaces, rupture of lumen of gland, and proliferation of epithelial cells into the surrounding stroma.

As illustrating a mistake that may be made in connection with ulcerating processes, I would cite a case recently referred to Dr. C. M. Robertson's clinic—a man, 34 years of age, presenting a large ulcer in the region of the soft palate, of six weeks' duration. Naturally the first thought of the clinician was of its being syphilis, but infection being so strongly denied by the patient, and no signs of primary or secondary lesions being detectable, it was set aside for the time being. Examination for tubercle bacilli was negative, tuberculosis of the respiratory tract was not to be detected, and so epithelioma was determined upon, especially as the edges of the ulcer showed a marked proliferation. A small piece, one-eighth of an inch square, was removed from the proliferating edge and subjected to microscopic examination. Section revealed a downgrowth of epithelium from the surface, and two areas of epithelial cells away and separate from the surface, from which it was essential to say that the picture indicated epithelioma.

In the meantime an antisypilitic treatment had been instituted and the ulcer began to heal rapidly, thus plainly indicating the mistake—one that, in fact, is often made in superficial examination of proliferating epithelial processes, where the direction in which a section is cut may give misleading microscopic pictures resembling epithelial proliferations into the deeper tissues, and emphasizing most strongly the obtaining of deeper sections from representative portions of the growth for diagnostic purposes.

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CONTAGION OF HERPES TONSURANS.—Several cases of herpes tonsurans were traced to the barber shop and through one customer to his dog, which had become infected by a monkey in the same house. Berger, who reports the occurrence in the *Derm. Chl.* for April, arrested the epidemic by prompt destruction of the infected articles in the barber shop. He suggests that stricter hygienic measures be exacted of barbers, who should raise their prices to correspond, and he also warns against the fondling of household pets.

EXPERIMENTS AND OBSERVATIONS IN SCARLET FEVER.*

BY W. K. JAKUES, M.D.

CHICAGO.

Since Chicago has achieved the distinction of being a great city, scarlet fever, in forms more or less severe, has been present. During the summer and autumn of 1897, Dr. I. N. Abt found it prevalent in a light form among the poorer classes of Poles and Bohemians in certain parts of the city. The cases were so light that physicians were seldom called, and no intelligent action was taken to restrict contagion. An epidemic resulted. The health department, while realizing the danger, was crowded by more serious matters, and the afflicted communities enjoyed the blessing of becoming immunized while the disease was in its mildest form. From these localities the fever has gradually spread until it has included the entire city.

In the autumn of 1898, when the reported cases of scarlet fever were greatly increased, Dr. Wynkoop of the city laboratory, while examining a culture from a scarlet fever patient, sent him by Dr. Findley, noticed a coccus which he first took to be a form of the pus coccus. But on growing, it manifested such peculiar characteristics that he began to pursue a careful study of the germ in the laboratory. At a certain stage of its development it became a large coccus, the center of which stained in the shape of a double crescent. While this germ was still under observation by Dr. Wynkoop, Dr. Class described his diplococcus scarlatinæ, in a paper before the Chicago Medical Society. While Dr. Wynkoop used the term "crescent" and Dr. Class "diplococcus," I concluded, after a study of many cultures from scarlet fever cases, that both were different forms of the same germ. This attempt to name an organism from some particular stage of its development was responsible for the uncertainty concerning it.

This germ has a wide morphology. Sometimes one stage and then another will become accentuated, according to environment and nutrition. Sometimes conditions are favorable to its growth in chains and the culture will show the streptococcus form. In another case it will grow as a staphylococcus, and in still another as a diplococcus. Again it becomes oblong and almost a bacillus. Early bacteriologists attempted to classify micro-organisms according to shape and arrangement, and they were divided into families of streptococci, staphylococci and bacilli, etc., but in this case we have a germ that may be either or all.

Bacteriology is still too young for us to be bound too strongly by precedent. Professor Koch formulated what he considered the law to which the causative germ of a disease should conform. While this law is applicable to some diseases, many more do not fulfill all the requirements, yet experience is demonstrating that germs are the essential causes of disease in those which do not conform as well as in those which do.

As above stated, the morphology of this germ, which I have been finding in scarlet fever, is one of its most interesting features. The size of the coccus depends on its environment and the medium on which it grows. In the same culture, it will sometimes vary from the smallest point observable under a one-twelfth oil-emersion to a coccus one-third the diameter of a red corpuscle. It appears that these cocci multiply by division, and that the multiplication takes place in various sizes of the germs. When inoculated on a culture-medium, they usually grow to the favorable dividing point and then

*Read before the Society of Internal Medicine, Chicago, Feb. 27, 1900